(b) screening or selecting the products of a) for a desired property; and

(c) recovering recombinant DNA substrate molecules from (b).

A further aspect of the invention is a method for evolving a DNA substrate sequence encoding a protein of interest, wherein the DNA substrate comprises a vector, the vector comprising single-stranded DNA, the method comprising:

(a) providing single-stranded vector DNA and a library of mutants of the DNA substrate sequence;

(b) annealing single stranded DNA from the library of (a) to the single stranded vector DNA of (a);

(c) transforming the products of (b) into a host;

(d) screening the product of (c) for a desired property; and

(e) recovering evolved DNA substrate DNA from the products of (d).

Brief Description of the Drawings

Figure 1 depicts the alignment of oligo PCR primers for evolution of bovine calf intestinal alkaline phosphatase.

Figures 2A-2E depict the alignment of alpha interferon amino acid and nucleic acid sequences.

Description of the Specific Embodiments

The invention provides a number of strategies for evolving polypeptides through recursive recombination methods. In some embodiments, the strategies of the invention can generally be classified as "coarse grain shuffling" and "fine grain shuffling." As described in detail below, these strategies are especially applicable in situations where some structural or functional information is available regarding the polypeptides of interest, where the nucleic acid to be manipulated is large, when selection or screening of many recombinants is cumbersome, and so on. "Coarse grain shuffling" generally involves the exchange or recombination of segments of nucleic acids, whether defined as functional